REMARKS

The applicants thank the Examiner for his careful attention to this matter, and submit that the claims as they currently stand are in condition for immediate allowance.

Rejections Under 35 U.S.C. § 112

Claims 1-2, 5, 16, 27, 32-33, 38, 41, 44, 58-59, and 81 are rejected under 35 U.S.C. § 112, para. 2, as indefinite for failing to particularly point out and distinctly claim that subject matter that the applicants regard as their invention.

With respect to claims 1-2, 27, 32-33, 41, 58-59, and 81, the Office Action indicates that the phrase "substantial" renders the claims indefinite because it is not clear how the light is directed onto the detector pixel. Claim 1 notes that the sampling position is set up "so that the source light that touches a chip address on the sample surface is substantially directed onto at least one detector pixel with an address that is correlated to the chip address." The pending application describes (and shows in the Figures) how the sample and the detector are arranged (in some embodiments with intervening lenses) so that the light is substantially directed onto at least one detector pixel.

For example, the application indicates that "direct mapping" of a member of a DNA array to a limited number of pixels in a sensor array is possible. Application, page 10. As illustrated in Figure 1, a mapping lens 3 can acquire the image from a sample and focus the image onto a detector. As illustrated in Figure 2, light may be passed through a chip 14, and a detector may be placed immediately behind the chip and in close proximity to it. In this manner, the light emitted from the chip has little space in which to disperse or to otherwise move; as a result, the light from a chip address is directly mapped to the detector. The arrangements of Figures 3A and 3B provide similar functionality. Other embodiments that show how direct mapping may be obtained are shown in Figures 5 and 6. Figure 7 shows that a mapping lens that incorporates a dichroic mirror can be used to focus light onto a detector so that the pixels of DNA on a DNA chip are mapped onto the detector pixels of a detector. Figures 8 and 9 show yet further

embodiments. At bottom, the pending application shows multiple examples for directing light onto a detector pixel.

There is also nothing indefinite about using relative terms such as "substantially" in a claim, and it is a commonly accepted practice. *Prima Tek II, L.L.C. v. Polypap*, 318 F.3d 1143, 65 USPQ2d 1818 (Fed. Cir. 2003) (reciting a fold that was "substantially bonded via [a] means for forming [a] crimped portion."); *Verve, LLC v. Crane Cams, Inc.*, 311 F.3d 1116, 65 USPQ2d 1051 (Fed. Cir. 2002) (rejecting argument that claim phrase "substantially constant wall thickness" is indefinite); *LNP Engineering Plastics, Inc. v. Miller Waste Mills, Inc.*, 275 F.3d 1347, 61 USPQ2d 1193 (Fed. Cir. 2001) (claim recited "substantially wetted"); *Ecolab, Inc. v. Envirochem, Inc.*, 264 F.3d 1358, 60 USPQ2d 1173 (Fed. Cir. 2001) ("substantially uniform"); *Glaxo Group Ltd. v. Ranbaxy Pharma., Inc.*, 262 F.3d 1333, 59 USPQ2d 1950 (Fed. Cir. 2001) ("substantially amorphous"); *Biotec Biologische Naturverpackungen GmbH & Co. KG v. Biocorp, Inc.*, 249 F.3d 1341, 58 USPQ2d 1737 (Fed. Cir. 2001) ("substantially water free"); *KCJ Corp. v. Kinetic Concepts, Inc.*, 223 F.3d 1351, 55 USPQ2d 1835 (Fed. Cir. 2000) ("substantially uniform airflow therethrough"). As a result, the applicants respectfully suggest that claim 1 is definite and is in condition for immediate allowance. The remaining rejected claims (claims 2, 5, 16, 27, 32-33, 38, 41, 44, 58-59, and 81) are dependent on claim 1 or recite similar limitations, and are in condition for allowance for the reasons stated above.

With respect to claims 5 and 16, the Office Action indicates that there is insufficient antecedent basis for the feature "the optical fiber." The applicants have amended claims 5 and 16 to overcome this rejection, and ask for prompt allowance of these claims.

With respect to claim 38, the applicants have cancelled this claim.

With respect to claim 44, the applicants have amended this claim to overcome the rejection.

Rejections Under 35 U.S.C. § 103 over King in light of Anderson

Claims 1-26, 27-38, 41-51, and 54-65 stand rejected under 35 U.S.C. § 103 over King et al. (U.S. Pat. 5,633,724) in view of Anderson (U.S. Pat. 4,088,561). Claims 1, 27, and 41 are the independent claims of this group. Applicants have amended these claims to morely clearly recite the chip holder feature.

King et al. discusses "Evanescent Scanning of Biochemical Array." The patent describes the desirability of reflecting light internally to a structure that holds a sample so as to create an "evanescent electromagnetic field" near a surface 112. *See* King et al., Col. 5, lines 18-22. An array of molecular tags is provided on the surface. *Id.*, lines 14-16. Although total internal reflection occurs at the surface so that none of the incident light passes through the surface, *id.*, lines 18-21, the evanescent field excites the tags so that they create an optical signal 116 on the side of surface 112 on which none of the incident light appears. An optical detection system 120 is provided on that same side. The King et al. patent distinguishes its system, whereby the incident light appears only on the upstream or input side of the sample, from simpler "direct illumination" systems that can create problems wherein the incident light drowns out the emitted light from the sample (i.e., has a low signal-to-noise ratio), *see* King et al., Col. 1, line 61 to Col. 2, line 7.

Amended claim 1 recites a detecting device that comprises a nucleic acid chip holder configured to receive a nucleic acid chip (which has a flat sample surface and an opposed surface, with a nucleic acid sequence immobilized to a particular chip address) and keep the chip in a sampling position, an optical filter, an electronic light detector array having detector pixels located at particular addresses, and a light source, wherein the sampling position places the sample surface in a well-defined spatial relationship relative to the array so that the source light that touches a chip address is substantially directed onto at least one detector pixel with an address that is correlated to the chip address. As noted above, the patent shows multiple examples of devices in which source light is directed to the detector. The central goal of King et al., in contrast (and as indicated above), is to *prevent* any source light from appearing anywhere on the detector side of the sample, for fear of corrupting the signal. Thus, not only does King et al. fail to teach or disclose the device recited in claim 1, it actually teaches away from such a device.

In addition, the Office Action recognizes that King et al. does not disclose a filter. The Office Action opines that it would have been obvious to modify King with a filter to filter out unwanted light. First, there is no support for the conclusion that it would have been obvious to modify King, so there is no prima facie basis for the rejection. *See In re Lee*, 277 F.3d 1338, 61 USPQ2d 1430 (Fed. Cir. 2002) (noting that Board must provide explicit factual support for

obviousness conclusions). Second, there simply is no motivation to modify King et al. so as to use a filter as recited in pending claim 1. Rather, because King uses an evanescent system, only light emitted from the tags appears on the detector side of the structure, so there is no need to filter other light. In fact, King et al. teaches away from such a structure by discussing the problems of having other light on the output side of the sample, as discussed above. As such, King et al. does not teach or suggest the features for which the Office Action cites it, and the applicants respectfully request that the rejection be withdrawn for this reason.

The Office Action relies on Anderson as disclosing a sample holder 39. Anderson discusses an "Apparatus for Electrophoresis Separation." As the Office Action admits, the sample holder 39 comprises two rigid plate members 45 that are hinged together, and that may be placed vertically in slots of a reservoir containing a buffer solution. Thus, an electrophoresis separation process may occur if a potential is applied to the solution. The application has nothing to do with imaging of a biological sample in a particular position; rather, it is directed toward classic electrophoresis, where the positioning of the plates is not important as long as they sit are immersed in the solution. Thus, as an initial matter, Anderson is directed to a totally different problem than is claim 1, and Anderson is non-analogous art which cannot be used to make a rejection. *See Jurgens v. McKasy*, 927 F.2d 1552, 18 USPQ2d 1031 (Fed. Cir. 1991) (noting that nonanalogous art "has no bearing on the obviousness of the patent claim.").

In addition, the structure of Anderson is a dual-plate structure through which a sample is designed to move. The separation of constituents within a sample is the way that electrophoresis works. In contrast, pending claim 1 recites that sequences of nucleic acides are immobilized to a chip. In this manner, the individual addresses of nucleic acids may be imaged with good resolution and predictability. The movement of the constituents in Anderson, and the use of two separate plates (each having its own refractive index), would interfere with the imaging. Thus, Anderson does not fill in the gaps that appear in King et al., and claim 1 is in allowable form for this reason also.

In addition, there is no motivation to combine King et al. and Anderson so as to create the invention of pending claim 1, and there is no motivation to modify what is disclosed in either reference so as to achieve what is recited in claim 1. Rather, even if one assumes that the references together teach all that is recited in pending claim 1, their combination is an improper

hindsight reconstruction that uses the applicant's claim as a road map to assist in picking and choosing elements from the references. *See, e.g., In re Kotzab*, 217 F.3d 1365, 55 USPQ2d 1313 (Fed. Cir. 2000) (faulting the Examiner and Board for falling into the "hindsight trap."); *Al-Site Corp. v. VSI Int'l, Inc.*, 174 F.3d 1308, 50 USPQ2d 1161 (Fed. Cir. 1999). For this reason also, the applicants submit that claim 1 is in condition for allowance, and request such prompt allowance.

Independent claims 27 and 41 also recite a nucleic acid chip holder configured to receive a nucleic acid chip and keep the chip in a sampling position, and an electronic light detector array, wherein the sampling position places the chip's sample surface at a well-defined position relative to the array. In claim 27, source light that touches a chip address is substantially directed onto at least one detector pixel with an address that is correlated to the chip address. In claim 41, light leaving a chip address is substantially directed onto at least one detector pixel with an address that is correlated to the chip address. As noted above, King et al. teaches that source light should not even appear on the downstream side of the sample, and Anderson does not disclose or suggest any sort of chip holder for imaging purposes, let alone the chip holder as recited in these claims. Because each of these independent claims is patentably distinct from the applied reference, the applicants respectfully request withdrawal of the rejection and allowance of all the claims, both independent and dependent.

The dependent claims differ from the cited references in additional ways. For example, dependent claims 2-3, 28-29, and 42-43 recite particular correlations between chip addresses and detector pixels. The Office Action contends that such a disclosure is inherent in Anderson et al. However, King et al. actually shows wide disperal of optical signal 116, so Anderson et al. does not disclose or suggest what is recited in these dependent claims. Claims 4-5 recite that light leaving the sample surface passes through the chip thickness or the optical filter. As indicated above, King et al. prevents any light from passing through layer 112, and instead excites tags that are on the layer using an evanescent field. As such, light from the sample does not pass through any chip, and there would be no need for an optical filter in King et al., as discussed above. Claims 6-9, 44-46, and 62 recite mapping lens or optical lenses used to map an image of the sample surface. Again, the Office Action admits that King et al. fails to disclose this feature, but maintains that it would, nonetheless, have been obvious. The rejection is, therefore, first

improper because there is no evidentiary support for the conclusion of obviousness; in addition, King et al. does not even suggest the need to map an image onto the detector, so the applicants submit that the claims are allowable for this reason also. As another example, claims 16-19 recite that the chip itself comprise certain components of the device (e.g., an optical filter or a mapping lens); there is absolutely no teaching or suggestion in the references to make a chip perform as a filter or mapping lens. Claim 20-26, 34, and 60 recite that certain components of the system are in direct physical contact. As the application indicates, such direct contact can allow for the direct mapping of sample positions to detector pixels. As discussed above, Anderson has no mapping at all (and no direct contact) because it is directed to a wholly different problem than imaging of a sample, and King et al. shows the dispersal of optical signal 116 over a space between the sample and the detector, so it too fails to teach or even suggest direct contact.

Rejections Under 35 U.S.C. § 103 over King in light of Anderson and Lakowicz

Claims 78-87 stand rejected under 35 U.S.C. § 103 over King et al. (U.S. Pat. 5,633,724) in view of Anderson (U.S. Pat. 4,088,561) and Lakowicz (WO 99/36578). Claim 78 is the independent claim of this group.

Claim 78 recites a polynucleic acid chip having a top sample surface that has immobilized nucleic acid sequences attached thereto, and an opposed surface, where the chip is made of light-transmitting material. As indicated in the application, the light-transmitting nature of the chip allows source light or light from the sample to pass through the chip on its way to the detector array.

As already discussed above, King et al. intentionally blocks all light at surface 112, so it teaches away from claim 78. Also, as discussed above, Anderson has nothing to do with imaging or light at all, so it is non-analogous and irrelevant to the inquiry here. Lakowicz discusses fluorescence in situ hibridization (FISH) with metal-ligand complexes to detect the presence of a nucleic acid. The metal-ligand complex is coupled to a nucleic acid sequence to form a mixture. *See* Lakowicz, page 5, line 17 to page 6, line 2. The Office Action does not cite, and the applicants are not aware of, any reference in Lakowicz to the fixing of any sample to a chip or any sort of imaging or light transmission through a chip. Thus, Lakowicz does not

add anything to either King et al. or Anderson. As a result, the applicants respectfully suggest that the rejection be withdrawn, and claims 78-87 be allowed.

The dependent claims differ even more from the applied references. For example, claims 79 and 82 recite that the chip comprises an optical filter. As discussed above, neither King et al. nor Anderson disclose or suggest such a structure. And Lakowicz, which does not discuss any sort of chip at all, of course cannot disclose or suggest such a structure. Claims 83-87 recite that the chip comprises an optical lens. For the reasons just discussed, none of the applied references either teaches or suggests such a feature. For these reasons also, each of the rejections should be withdrawn, and the claims allowed to issue promptly.